SETH J. COREY, M.D., CHILDREN'S HOSPITAL OF PITTSBURGH $31,300

Signalling Partners for Myeloid Growth Factor Receptors

Two hormones, granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF), regulate the production and activity of white blood cells. Signals are generated by receptors that specifically recognize and bind these growth factors. These signals then trigger a variety of biochemical responses that lead to cell division, maturation, or activation. When these growth signalling pathways go awry, leukemia arises. By identifying the molecules which interact with the GM-CSF or G-CSF receptors, we will better understand normal and abnormal white cell properties. Some forms of human or animal leukemia have already been identified where genetic changes have occurred in these signalling molecules. Our studies will examine specific receptor-enzyme interactions and will identify new binding partners for the GM-CSF and G-CSF receptors by screening a collection of genes that make up human white blood cells.

JOHN H. BUSHWELLER, Ph.D., DARTMOUTH COLLEGE $35,000

NMR Structural Studies of Core-binding Factor Proteins

We are attempting to determine the three-dimensional structures of two proteins known to play an important role in the development of a number of specific forms of leukemia. Knowledge of the three-dimensional structures of these proteins will allow us to better understand how they function at the molecular level. In addition, knowledge of the three-dimensional structures of these two proteins may allow us to design very specific drugs that would bind to these proteins and inhibit their function, thereby providing a possible treatment for these forms of leukemia.

JENNIFER MARTIN, Ph.D., PURDUE UNIVERSITY $35,000

Signal Transduction by the LMP-1 Oncoprotein of Epstein-Barr Virus in Human B-cell Transformation

Epstein-Barr Virus (EBV) in an ubiquitous human herpesvirus associated with two lymphoid tumors and an epithelial tumor. Severely immunocompromised persons (AIDS patients and transplant recipients) are at high risk for the development of fatal EBV-dependent tumors. Infection of the target B-lymphocyte by EBV results in uncontrolled growth, a hallmark of the malignant cell. These cells are immortal. The ability of EBV to immortalize B-lymphocytes is critical for its contribution to lymphoid tumorigenesis. The focus of the research described in this proposal is to identify interactions between the virus and the cell resulting in B-lymphocyte immortalization. Identifying mechanisms involved in immortalization by EBV is essential for understanding the contribution of EBV to tumorigenesis, and is likely to provide insights into the processes governing the uncontrolled growth of other virally and nonvirally induced malignancies. Furthermore, understanding the interaction between EBV and the cell that results in immortalization as described in this proposal is critical for the rational development of therapies for EBV-associated malignant and nonmalignant diseases.